REMARKS

The office action dated July 7, 2006 has been carefully considered. This Amendment, taken with the following remarks, is believed sufficient to place the present application in condition for allowance. Reconsideration and an early allowance are respectfully requested.

Applicants appreciate the analysis as to why claim 20 should be included within the scope of the non-elected claims of group II-III and have withdrawn claim 20 from examination accordingly.

Applicants acknowledge and appreciate the entry of the April 25, 2006 amendment and substitute sequence listing to the specification.

Claim 15 has been amended to clarify that it is directed to an isolated nucleic acid, and that the isolated nucleic acid has the recited mutation at position 116 of the nucleic acid set forth as SEQ ID NO: 1. Claim 21 has been added and is directed specifically to the isolated nucleic acid comprising the sequence as set forth in SEQ ID NO: 7. As it is believed that this Amendment does not involve the addition of new matter, entry and consideration are respectfully requested.

Claims 1-21 are pending, and claims 15, 18, 19 and 21 are currently subject to examination.

35 U.S.C. § 112, first paragraph; written description

Claims 15, 18 and 19 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner asserts that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the art that the inventors had possession of the claimed invention as of the filing date.

In particular, the Examiner asserts that claim 15 "appears to encompass any nucleic acid comprising SEQ ID NO: 7, but which is polymorphic at any position with respect to SEQ ID NO: 7, or polymorphic on either side of SEQ ID NO: 7, as well as any fragments from any source so that the claims therefor encompass an extremely large genus of nucleic acid variants, homologs and mutants of SEQ ID NO: 7, from any source, while "the specification , however, has only described a single polymorphism within SEQ ID NO: 1, to to G at position 116, which is associated with dilated cardiomyopathy (DCM) when present as homozygous mutation." The Examiner notes that SEQ ID NO: 7 encodes the full length 52 amino acid human phospholamban protein with a mutation at position 116 which replaces the T in SEQ ID NO: 1 to a G, but asserts that the claim language encompasses any nucleic acid comprising a polymorphism at any position of SEQ ID NO: 7, etc, for which no written description is provided.

With respect to new claims 18 and 19, the Examiner specifically asserts that they encompass any mutant, variant or homolog phospholamban nucleic acid from any source which comprises a mutation that results in deletion of a cleavage site for a restriction endonuclease as well as any mutation which results in an L39X mutation in any phospholamban sequence. The Examiner states "Other than providing the sequence of SEQ ID NO: 1 and defining the T to G mutation at position 116 of SEQ ID NO: 1, the specification does not describe the attributes needed for a nucleic acid to be generally identified as 'a phospholambban plymorphism.'" Further, with

respect to the L39X mutation, the Examiner states that without a reference for the number "39," the claim encompasses any nucleic acid which would encode a stop codon at position 39 of any phospholamaban mutant, variant, or homolog sequence from any source.

In the "Response to Arguments" found on page 8 of the Office Action, the Examiner notes that "the only polymorphism taught in the specification was a T to G mutation at position 116 of SEQ ID NO: 1. This rejection is traversed and reconsideration is respectfully requested.

Instant claim 15 is directed to an isolated nucleic acid comprising a phospholamban polymorphism, comprising a G to T mutation at position 116 of a nucleic acid having a sequence of nucleic acids set forth as SEQ ID NO: 1. This recitation makes it clear that Applicants are claiming an isolated nucleic acid, and that the nucleic acid comprises a polymorphism of phospholamban, and that the nucleic acid comprises a particular mutation of a sequence as set forth in SEQ ID NO: 1. Applicants believe that this recitation provides the particularity requested by the Examiner. Applicants do not intend to claim the genus having the scope as described by the Examiner.

As the Examiner noted, the present disclosure provides "the sequence of SEQ ID NO: 1 and defines the T to G mutation at position 116 of SEQ ID NO: 1," and therefore fully supports the subject matter of claim 15, as amended. Claims 18 and 19 have been amended to make them depend from independent claim 15, overcoming the Examiner's concern with a defined reference for the mutation.

Hence, the rejection of claims 15, 18 and 19 under 35 U.S.C. § 112, first paragraph, is overcome and reconsideration is respectfully requested.

35 U.S.C. § 112, second paragraph; definiteness

Claim 15 is further rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Specifically, the Examiner notes that the claim recites "an isolated phospholamban polymorphism fragment comprising SEQ ID NO: 1," and asserts that this "is confusing because the term 'comprising' is normally taken to mean the full sequence of SEQ ID NO: 1 with any nucleotides on either side...[the context being]...unclear in this situation because the only mutation/polymorphism taught in the specification is at position 116 of SEQ ID NO: 1, wherein said position is a G instead of a T." The Examiner appears to object to the use of the term "polymorphism" as confusing, and questions whether the claim is intended to be drawn to an isolated nucleic acid as described, or to any nucleic acid which is polymorphic to the defined sequence. This rejection is traversed and reconsideration is respectfully requested.

The recitation of instant claim 15 is set forth above. Applicants submit that it is clear that it is drawn to an isolated nucleic acid comprising the recited sequence and not to any nucleic acid polymorphic to the recited sequence. The recited sequence reflects the polymorphism that is the subject matter of the invention. Applicants further submit that, consistent with accepted usage of the term "comprising," the inventive nucleic acids include those which have the recited polymorphism, with any nucleotides on either side, as well as those which may have other nucleic acid substitutions, deletions or additions, which do not impact the functional significance, as disclosed, of the mutation defining the instantly recited polymorphism.

As noted, instant claims 18 and 19 have been amended to be dependent from instant independent claim 15, thereby overcoming the lack of reference for the recited L39StopCodon.

Applicants submit, therefore, that the meanings of the claim terms are definite and the scope of the claim is readily ascertainable by a person of ordinary skill in the art. Hence, the rejection of claims 15, 18 and 19 under 35 U.S.C. § 112, second paragraph has been overcome and reconsideration is respectfully requested.

35 U.S.C. § 102

Claims 15 and 18 are rejected under 35 U.S.C. § 102(b) as being anticipated by Genbank Accession Number X15075 (deposited September 1993), and as evidenced by New England Biolabs, 1995 catalog, page 13, and by Genbank Accession number M60411, deposited January 1995. Specifically, the Examiner asserts that X15075 teaches mRNA for pig phospholamban which is polymorphic with respect to SEQ ID NO: 1 at 10 positions, and that Accession number M60411 teaches mRNA for human phospholamban which comprises SEQ ID NO: 1 and is polymorphic with SEQ ID NO: 7.

The recitation of claim 15, from which claim 18 depends, is set forth in detail, above. Applicants note that none of the 10 mutations occurring in the X15075 reference sequence comprises the T to G mutation at position 116 of SEQ ID NO: 1, and the M60411 reference sequence fails to include the recited mutation as well. The scope of Applicants' inventive nucleic acids is limited to those nucleic acids having this mutation, regardless of the presence of absence of other mutations or additional nucleic acids at either end of the

recited sequence. Hence, a reference nucleic acid cannot anticipate the presently inventive nucleic acids unless it comprises at least the mutation as recited in instant claim 15.

Anticipation under 35 U.S.C. § 102(b) requires the disclosure in a single prior art reference of each element of the claims under consideration, *Alco Standard Corp. v. TVA*, 1 U.S.P.Q.2d 1337, 1341 (Fed. Cir. 1986). The asserted reference nucleic acids fail to include the mutation as recited in independent claim 15 as defining the isolated nucleic acids of the invention. Hence, the rejection of claim 15, as well as dependent claim 18, under 35 U.S.C. § 102(b) has been overcome and reconsideration is respectfully requested.

Claims 15 and 18 are rejected under 35 U.S.C. 102 (a) as being anticipated by Kimura et al; Mol. Pharmacology, vol. 61, pages 667-673, 2002 ("Kimura"). Specifically, the Examiner asserts that the reference encompasses nucleic acids which are fragments of SEQ ID NO: 7, and which have polymorphisms with respect to SEQ ID NO: 7. The Examiner also objects that the claims appear to encompass fragments of the recited sequence, having no defined length. This rejection is traversed and reconsideration is respectfully requested.

Applicants admit to being puzzled as to why the Examiner appears focused on the length of the inventive sequences, yet ignores the defining limitation, that is, the presence of a mutation at a defined position, that position having a reference with respect to the wild type phospholamban. The instant claim encompasses polymorphisms of phospholamban defined by the presence of a particular mutation. Yet, the Examiner has yet to assert a

reference disclosing that mutation or the inventive polymorphism. Kimura fails to teach, disclose or otherwise suggest isolated nucleic acids comprising the recited mutation. Hence, Kimura cannot anticipate the present invention and the rejection of claims 15 and 18 under 35 USC 102(a) is overcome . Reconsideration is respectfully requested.

Applicants believe that the above represents a complete and effective response to the rejections of the present claims under 35 U.S.C. §§ 112, and 102. Hence, reconsideration and an early allowance are respectfully requested.

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